FILE 'HOME' ENTERED AT 13:25:09 ON 28 NOV 2003

=> file agricola biosis caplus caba
=> s lectin and cry?
L1 2061 LECTIN AND CRY?

=> s lectin and cryi?
L2 21 LECTIN AND CRYI?

=> duplicate remove l2
L3 18 DUPLICATE REMOVE L2 (3 DUPLICATES REMOVED)

=> d ti 1-18

L3 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Altered glycosylation of 63- and 68-kilodalton microvillar proteins in Heliothis virescens correlates with reduced Cry1 toxin binding, decreased pore formation, and increased resistance to Bacillus thuringiensis Cry1 toxins

L3 ANSWER 2 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
TI PCR detection of transgenic elements in feed raw material.

L3 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Linear transgene constructs lacking vector backbone sequences generate transgenic rice plants which accumulate higher levels of proteins conferring insect resistance

L3 ANSWER 4 OF 18 CABA COPYRIGHT 2003 CABI on STN
TI Detection of transgenic elements in feed materials by PCR method.

L3 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Novel primer pairs for detection of genetically engineered plant material in food

L3 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI PCR method for detecting recombinant DNAs from genetically modified crops and processed food

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Expression of multiple insecticidal genes confers broad resistance against a range of different rice pests

L3 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Fusion proteins comprising Bacillus thuringiensis **CryIA**(b,c) toxins and ricin B chain fragments and their pesticidal activities

L3 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Method for producing transgenic plants resistant to glyphosate herbicides

L3 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Detection of genetically modified soybeans and maize by the polymerase chain reaction method

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Partial purification and characterization of Bacillus thuringiensis Cry1A toxin receptor A from Heliothis virescens and cloning of the corresponding cDNA

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Expression of two insect-resistant genes **cryIA** (b&c)/GNA in transgenic tobacco plants results in added protection against both cotton bollworm and aphids

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Construction of plant expression vector harboring two insect-resistant genes and their expression in tobacco

L3 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI Factors affecting the binding of the Bacillus thuringiensis crystal protein, Cry1Ba, to Wiseana cervinata brush border membrane vesicles

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
TI The receptor for Bacillus thuringiensis **CryIA**(c) delta-endotoxin in the brush border membrane of the lepidopteran Manduca sexta is aminopeptidase N

L3 ANSWER 18 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 2
TI N ACETYLGALACTOSAMINE IS PART OF THE RECEPTOR IN INSECT GUT EPITHELIA THAT RECOGNIZES AN INSECTICIDAL PROTEIN FROM BACILLUS-THURINGIENSIS.

=> d bib abs 17 15 14 13 7

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1994:238222 CAPLUS
DN 120:238222
TI The receptor for Bacillus thuringiensis **CryIA**(c) delta-endotoxin in the brush border membrane of the lepidopteran Manduca sexta is aminopeptidase N
AU Knight, Peter J. K.; Crickmore, Neil; Ellar, David J.
CS Dep. Biochem., Univ. Cambridge, Cambridge, CB2 1QW, UK
SO Molecular Microbiology (1994), 11(3), 429-36
CODEN: MOMIEE; ISSN: 0950-382X
DT Journal
LA English
AB A 120 kDa glycoprotein in the larval midgut membrane of the lepidopteran Manduca sexta, previously identified as a putative receptor for Bacillus thuringiensis CrylA(c) .delta.-endotoxin, has been purified by a combination of protoxin affinity chromatog. and anion exchange chromatog. In immunoblotting expts., the purified glycoprotein has the characteristics predicted of the receptor: it binds CrylA(c) toxin in the presence of GlcNAc but not GalNAc; it binds the **lectin** SBA; but it does not bind **CryIB** toxin. N-terminal and internal amino acid sequences obtained from the protein show a high degree of similarity with the enzyme aminopeptidase N (EC 3.4.11.2). When assayed for aminopeptidase activity, purified receptor prepns. were enriched 5.3-fold compared to M. sexta brush border membrane vesicles. The authors propose that the receptor for CrylA(c) toxin in the brush border membrane of the lepidopteran M. sexta is the metalloprotease aminopeptidase N.

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:805078 CAPLUS
DN 133:1270
TI Construction of plant expression vector harboring two insect-resistant genes and their expression in tobacco
AU Wang, Zhibin; Guo, Sandui
CS Lab. of Biochemistry and Molecular Biology, Biotechnology Research Center, Chinese Academy of Agricultural Sciences, Beijing, 100081, Peop. Rep. China
SO Gaojishu Tongxun (1999), 9(11), 001-006
CODEN: GTONE8; ISSN: 1002-0470
PB Gaojishu Tongxun Zazhishe
DT Journal
LA Chinese
AB A synthesized Bacillus thuringiensis insecticidal crystal protein gene **cryIA** and synthesized GNA (the mannose specific **lectin** from snowdrop (Galanthus nivalis)) were inserted into plasmid pBI121.1 to obtain plant expression vector pGW4BAI, in which each gene controlled by several regulation elements for initiation and termination of transcription and enhancement of translation. Leave stripes of Nicotiana tabacum var. K326 were transformed with Agrobacterium tumeficiens strain LBA4404 harboring the plant expression vector. PCR and Southern blotting anal. showed the foreign **cryIA** and GNA gene being inserted into the genome of transformed tobacco plants. Leaf disk bioassay against cotton bollworm (H. armigera) showed transgenic tobacco plants having high insecticidal activity. Inhibition of aphid population in leaf disk bioassay against Myzus persicae showed fecundity of transgenic plants being lower than that of on untransformed plants; the aphid population on the transgenic tobacco plants being 25-70% of that of on untransformed tobacco plant. Through the two bioassay against H. armigera and M. persicae, several transgenic tobacco plants showing high insect resistant activities to both pests were obtained.

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:800322 CAPLUS
DN 132:289336
TI Expression of two insect-resistant genes **cryIA** (b&c)/GNA in transgenic tobacco plants results in added protection against both cotton bollworm and aphids
AU Wang, Zhibin; Guo, Sandui
CS Laboratory of Biochemistry and Molecular Biology, Biotechnology Research Center, Chinese Academy of Agricultural Sciences, Beijing, 100081, Peop. Rep. China
SO Chinese Science Bulletin (1999), 44(22), 2051-2058
CODEN: CSBUEF; ISSN: 1001-6538
PB Science in China Press
DT Journal
LA English
AB The synthesized Bacillus thuringiensis insecticidal protein gene **cryIA** (b&c) and the synthesized gene GNA, (the mannose specific **lectin** from snowdrop (Galanthus nivalis)), tumefaciens have been

inserted into plant expression vector pGW4BAI. Leave stripes of Nicotiana tabacum var. K326 have been transformed with Agrobacterium tumefaciens strain LBA4404 harboring the plant expression vector. 28 Kanamycin resistant tobacco plants have been obtained. PCR and Southern blot analyses show that the foreign **cryIA** and GNA genes have been inserted into the genome of transformed tobacco plants. Hemagglutination assays show that GNA has a functional activity. Leaf disk bioassays against cotton bollworm (H. armigera) show that the transgenic tobacco plants have a high insecticidal activity. The inhibition of aphid population in leaf disk bioassays against Myzus persicae shows that the fecundity of aphid on transgenic plants is lower than that on untransformed plants; the aphid population on the transgenic tobacco plants is 25%-70% that on untransformed tobacco plants. ELISA anal. of **CryIA** protein in tobacco leaves provides similar data to bioassay results. Through the two bioassays against H. armigera and M. persicae, several transgenic tobacco plants showing high insect-resistant activities to both pests have been obtained.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1999:721555 CAPLUS
DN 132:47878
TI Partial purification and characterization of Bacillus thuringiensis Cry1A toxin receptor A from Heliothis virescens and cloning of the corresponding cDNA
AU Oltean, Daniela I.; Pullikuth, Ashok K.; Lee, Hyun-Ku; Gill, Sarjeet S.
CS Environmental Toxicology and Graduate Programs and Department of Neuroscience, University of California, Riverside, CA, 92521, USA
SO Applied and Environmental Microbiology (1999), 65(11), 4760-4766
CODEN: AEMIDF; ISSN: 0099-2240
PB American Society for Microbiology
DT Journal
LA English
AB Although extensively studied, the mechanism of action of insecticidal Bacillus thuringiensis Cry toxins remains elusive and requires further elucidation. Toxin receptors in the brush border membrane demand particular attention as they presumably initiate the cascade of events leading to insect mortality after toxin activation. The 170-kDa Cry1Ac toxin-binding aminopeptidase from the tobacco budworm (Heliothis virescens) was partially purified, and its corresponding cDNA was cloned. The cDNA encodes a protein with a putative glycosyl phosphatidylinositol anchor and a polythreonine stretch clustered near the C terminus with predicted O-glycosylation. Partial purifn. of the 170-kDa aminopeptidase also resulted in isolation of a 130-kDa protein that was immunol. identical to the 170-kDa protein, and the two proteins had identical N termini. These proteins were glycosylated, as suggested by soybean agglutinin **lectin** blot results. Cry1Ac toxin affinity data for the two proteins indicated that the 130-kDa protein had a higher affinity than the 170-kDa protein. The data suggest that posttranslational modifications can have a significant effect on Cry1A toxin interactions with specific insect midgut proteins.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:307179 CAPLUS
DN 136:65624
TI Expression of multiple insecticidal genes confers broad resistance against a range of different rice pests
AU Maqbool, Shahina Bano; Riazuddin, Sheikh; Loc, Nguyen Thi; Gatehouse, Angharad M. R.; Gatehouse, John A.; Christou, Paul
CS Molecular Biotechnology Unit, John Innes Centre, Norwich, NR4 7UH, UK
SO Molecular Breeding (2001), 7(1), 85-93
CODEN: MOBRFL; ISSN: 1380-3743
PB Kluwer Academic Publishers
DT Journal
LA English
AB We report the simultaneous introduction of three insecticidal genes (the Bt genes cry1Ac and cry2A, and the snowdrop **lectin** gene gna) into com. important indica rice varieties M7 and Basmati 370, by particle bombardment. Transgenic plants expressed Cry1Ac, Cry2A and GNA at different levels, either singly or in combination at 0.03-1%, 0.01-0.5% and 0.01-2.5% of total sol. protein, resp. The transgenes showed stable transmission and expression, and R1 transgenic plants provided significant ($p<0.01$) protection against three of the most important insect pests of rice: rice leaf folder (Cnaphalocrocis medinalis), yellow stemborer (Scirpophaga incertulas) and brown planthopper (Nilaparvata lugens). The triple transformants showed significantly ($p<0.05$) higher resistance to these insects than plants expressing single transgenes. Bioassays using the triple-transgenic plants showed 100% eradication of the rice leaf folder and yellow stem borer, and 25% redn. in the survival of the brown planthopper. The greatest redn. in insect survival, and the greatest redn. in plant damage, occurred in plants expressing all three transgenes. This approach maximises the utility of gene transfer technol. to introduce

combinations of genes whose products disrupt different biochem. or physiol. processes in the same insect, providing a multi-mechanism defense.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s ricin and cryi?
L4 1 RICIN AND CRYI?

=> d ti

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
TI Fusion proteins comprising Bacillus thuringiensis **CryIA**(b,c) toxins and **ricin** B chain fragments and their pesticidal activities

=> logoff hold
STN INTERNATIONAL SESSION SUSPENDED AT 13:32:06 ON 28 NOV 2003

FILE 'HOME' ENTERED AT 10:34:53 ON 12 DEC 2003

=> file agricola biosis caplus caba

=> s diphtheria and b and bind?
L1 480 DIPHTHERIA AND B AND BIND?

=> duplicate remove l1
L2 352 DUPLICATE REMOVE L1 (128 DUPLICATES REMOVED)

=> s l2 and review
L3 7 L2 AND REVIEW

=> d ti 1-7

L3 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Complete clinical resolution of peripheral T-cell lymphoma (Lennert's variant) with denileukin diftitox (ONTAK(R)).

L3 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Involvement of small GTPases in the regulation of smooth muscle contraction.

L3 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI ACTION AND PRODUCTION OF **DIPHTHERIA** TOXIN.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Translocation of **diphtheria** toxin across cellular membranes

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Protein engineering of DAB-IL-2 fusion toxins to increase biological potency

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Transport of hydrophilic proteins across biological membranes: use of **diphtheria** toxin as a model protein

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
TI Biophysical properties of **diphtheria** toxin fragment **B** in correlation to its **binding** ability to eukaryotic cell membranes

=> d bib abs 4 6 7

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1996:655085 CAPLUS
DN 125:298250
TI Translocation of **diphtheria** toxin across cellular membranes
AU Olsnes, S.; Klingenberg, O.; Falnes, P. Oe.; Valdizan, E. M.; Lanzrein, M.; Wiedlocha, A.
CS Institute Cancer Research, Norwegian Radium Hospital, Oslo, 0310, Norway
SO Zentralblatt fuer Bakteriologie, Supplement (1996), 28(Bacterial Protein Toxins), 154-160
CODEN: ZBASE2; ISSN: 0941-018X
PB Fischer
DT Journal; General Review
LA English
AB A **review** with 18 refs. Transport of **diphtheria** toxin to the cytosol is initiated by **binding** of the **B** -fragment to specific cell surface receptors, the precursor of heparin **binding** EGF-like growth factor. Translocation of the A-fragment across cellular membranes is induced by low pH as obtained in endosomes or, artificially, by acidification of the extracellular medium. In the

latter case, translocation occurs from the cell surface. Introduction of an artificial internal disulfide bond in the toxin A-fragment prevented translocation in both systems. When the artificial disulfide was located near the N-terminal end of the A-fragment, the protein became stuck in a partially translocated state. Also when the disulfide was located C-terminally the interfragment disulfide was reduced, but in this case the A-fragment was released into the medium. The intrafragment disulfide was not reduced in either case. The data indicate that translocation is initiated by transfer of the interfragment disulfide to the cytosol.

L3 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1992:17238 CAPLUS
DN 116:17238
TI Transport of hydrophilic proteins across biological membranes: use of **diphtheria** toxin as a model protein
AU Madshus, I. H.; Moskaug, J. O.
CS Inst. Cancer Res., Norw. Radium Hosp., Oslo, 0310, Norway
SO Methodological Surveys in Biochemistry and Analysis (1991), 21(Cell Signalling: Exp. Strategies), 79-84
CODEN: MSBADU; ISSN: 0748-6715
DT Journal; General Review
LA English
AB A **review**, with 17 refs. Bacterial and plant toxins are the only examples of proteins known to enter the cytosol of eukaryotic cells when added in the medium. **Diphtheria** toxin (DT) has for several years been employed as a model protein in studies of protein translocation across biol. membranes. DT is synthesized as a single polypeptide chain by pathogenic strains of Cornybacterium diphtheriae, but the toxin is activated by proteolytic cleavage, yielding disulfide-linked fragments A and B. Entry can easily be assayed, because fragment A has ADP-ribosyl transferase activity, which inactivates elongation factor 2. Fragment B is responsible for receptor **binding** and membrane interaction. Both native DT and fragment B alone form cation-selective channels, measured as an influx of 22Na+, when cells with surface-bound protein are exposed to low pH. The capacity for channel formation serves as a measure of whether the protein can be inserted properly into the membrane, and can be used in functional tests for DT mutants and DT-derived fusion proteins.

L3 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1980:175217 CAPLUS
DN 92:175217
TI Biophysical properties of **diphtheria** toxin fragment B in correlation to its **binding** ability to eukaryotic cell membranes
AU Lambotte, P.; Falmagne, P.; Capiau, C.; Ruysschaert, J. M.; Dirkx, J.
CS Lab. Chim. Biol. Biophys., Univ. Etat Mons, Mons, Belg.
SO Archives Internationales de Physiologie et de Biochimie (1979), 87(5), 1041-2
CODEN: AIPBAY; ISSN: 0003-9799
DT Journal; General Review
LA English
AB A **review** with 8 refs.

=> d bib abs 1-3, 5

L3 ANSWER 1 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:152389 BIOSIS
DN PREV200200152389
TI Complete clinical resolution of peripheral T-cell lymphoma (Lennert's variant) with denileukin diftitox (ONTAK(R)).
AU Bernstein, Zale P. [Reprint author]; Miller, Kena [Reprint author]; Barcos, Maurice P.
CS Oncology, Roswell Park Cancer Center, Buffalo, NY, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 238b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002
AB Peripheral T-cell lymphoma (PTCL), Lennert's variant, is known to follow a variable course and transform into an aggressive phase. The lymphoma cells tend to remain confined to lymph nodes; extranodal or cutaneous involvement is rare. Current therapies include doxorubicin-based combination chemotherapy. Patients generally respond poorly, relapse rate is high, and overall survival is poor. ONTAK (denileukin diftitox) is a cytotoxic fusion protein that contains the enzymatic and translocation domains of the **diphtheria** toxin, bound to human interleukin-2 (IL-2). ONTAK selectively **binds** to the IL-2 receptor and is internalized into the cell via endocytosis. Ultimately cell death occurs

as the diphtheria toxin enters the cytoplasm of the cell and acts to inhibit protein synthesis. Expression of the interleukin-2 receptor on the surface of various malignant cells of lymphoid origin forms the rationale for use of ONTAK in the T-cell non-Hodgkin lymphomas. ONTAK has been used for T-cell lymphomas that do not have cutaneous involvement, but data are very limited. LeMaistre, et al previously described a complete remission in one patient with diffuse large-cell immunoblastic (Lennert's) NHL (Blood, 91, 2, 1998). A 51-year-old male initially diagnosed with Hodgkin's disease had successful induction to remission with 6 cycles of ABVD. He was referred to our institution when his adenopathy recurred. At that time review of original pathology led to a revision of his initial diagnosis to that of PTCL, Lennert's variant. He then received one cycle of DHAC and progressed, and was given ICE but continued to progress. A thorough clinical and radiologic evaluation at that time showed rapid progression of disease with severe pruritus, increased lymphadenopathy, splenomegaly, malaise and fatigue. The patient then received eight 5-day courses of ONTAK given every 21 days. Doses increased from an initial 9mcg/kg to 21 mcg/kg/day. Over the course of ONTAK therapy, the patient showed improved appetite, weight stabilization, diminished fatigue, and resolution of rash and pruritus. Clinically the patient had complete resolution of his lymphadenopathy; however, the splenomegaly persisted. Adverse events included an episode of acute renal failure after the first cycle of ONTAK. Clinical response and chemical abnormalities suggested this may have been due to tumor lysis. Allopurinol and aggressive IV hydration were added to the drug regimen, and no further episodes of renal failure occurred. Other side effects were generally limited to the first 24 to 48 hours of each 5 day cycle. These included fevers, nausea and occasional hypotension (discontinuation of verapamil during course of ONTAK was effective in maintaining stable BP overall). Premedications included acetaminophen, dexamethasone, prochlorperazine, and aggressive IV hydration. As the patient's spleen appeared to have persistent disease, and he continued to have symptoms of splenomegaly (abdominal discomfort, early satiety), the patient elected to undergo splenectomy approximately 4 weeks after his eighth course of ONTAK. Pathological examination of his spleen suggested past but no definite present involvement by lymphoma. Flow cytometric analysis of this tissue revealed a high frequency of dead cells but without any evidence of T or B-cell malignancy. This experience suggests ONTAK may have some therapeutic benefit in non-cutaneous T-cell lymphomas.

L3 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1999:72681 BIOSIS
DN PREV199900072681
TI Involvement of small GTPases in the regulation of smooth muscle contraction.
AU Pfitzer, G. [Reprint author]; Arner, A.
CS Inst. Vegetative Physiologie, Univ. Koeln, Robert-Kochstr. 39, D-50931 Koeln, Germany
SO Acta Physiologica Scandinavica, (Dec., 1998) Vol. 164, No. 4, pp. 449-456. print.
CODEN: APSCAX. ISSN: 0001-6772.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
AB Neurohumoral stimulation of smooth muscle leads to an increased responsiveness of the myofilaments to Ca2+. This review provides a summary of the data that suggest that the signalling from the membrane-bound serpentine receptors to the contractile apparatus leading to the increase in Ca2+-sensitivity requires the activation of the Ras-related low molecular mass GTPase Rho. In smooth muscle permeabilized with alpha-toxin or beta-escin, the increase in force elicited by different agonists at fixed (Ca2+) (Ca2+-sensitization) can be inhibited by bacterial toxins (EDIN, and exoenzyme C3) which ADP-ribosylate and inactivate Rho proteins. Moreover, the agonist-induced increase in Ca2+-sensitivity can be mimicked by constitutively active recombinant Rho proteins. The physiological relevance of this mechanism is suggested by the fact that toxins that are internalized into intact cells (toxin B from C. difficile and a chimeric toxin (DC3B) consisting of C3 and the (non-catalytic) B fragment of diphteria toxin (inhibit the tonic phase of an agonist-induced contraction. Toxin B inhibits contraction without affecting the intracellular Ca2+-transient determined with fura-2. However, it inhibits phosphorylation of the regulatory light chains of myosin (MLC). Rho has been suggested to activate a Rho-associated kinase which in turn phosphorylates the myosin binding subunit of the myosin light chain phosphatase. This would lead to an increase in phosphorylation of MLC and hence of force at constant Ca2+. The Ca2+-sensitizing effect of agonists is also inhibited by tyrosine kinase inhibitors. This suggests the possibility that in smooth muscle, like in non-muscle cells, there is a cross-talk between Rho and tyrosine kinases.

L3 ANSWER 3 OF 7 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

AN 1975:132072 BIOSIS
DN PREV197559032072; BA59:32072
TI ACTION AND PRODUCTION OF **DIPHTHERIA** TOXIN.
AU UCHIDA T
SO Japanese Journal of Bacteriology, (1974) Vol. 29, No. 4, pp. 651-664.
CODEN: NSKZAM. ISSN: 0021-4930.
DT Article
FS BA
LA Unavailable

L3 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1993:99766 CAPLUS
DN 118:99766
TI Protein engineering of DAB-IL-2 fusion toxins to increase biological potency
AU Kiyokawa, Tetsuyuki; Williams, Diane P.; Snider, Catherine E.; Waters, Cory A.; Nichols, Jean C.; Strom, Terry B.; Murphy, John R.
CS Med. Cent., Boston Univ., Boston, MA, 02118, USA
SO Annals of the New York Academy of Sciences (1991), 636(Antigen Clone-Specific Immunoregul.), 331-9
CODEN: ANYAA9; ISSN: 0077-8923
DT Journal; General Review
LA English
AB A **review**, with 43 refs. The genetic replacement of either the native **diphtheria** toxin or Pseudomonas exotoxin A receptor **binding** domain with the eukaryotic cell receptor-specific polypeptide hormones or growth factor sequences has resulted in the development of a new class of biol. response modifier-the fusion toxin. The 1st of these fusion toxins, DAB486-interleukin-2 (IL-2), is currently in human phase I clin. trials and the early results clearly demonstrate that this mol. is safe, well-tolerated, and biol. active in the elimination of high-affinity IL-2 receptor-pos. leukemia and lymphoma cells without adverse side effect. DAB486-IL-2 is a bipartite fusion protein composed of **diphtheria** toxin fragment A and fragment B sequences to Ala486 linked to Pro2 through Thr133 of human IL-2. This chimeric protein is the product of a genetic fusion between a truncated gene encoding fragment A and the membrane-assocg. domains of fragment B of **diphtheria** toxin and a synthetic gene encoding human IL-2. DAB486-IL-2 has been shown to selectively **bind** to high-affinity IL-2 receptors, be internalized by receptor-mediated endocytosis, and facilitate the delivery of **diphtheria** toxin fragment A to the cytosol of target cells. Recent studies have defined the minimal size of fragment B that is required to deliver fragment A across the endocytic vesicle membrane in target cells, and defined the site of proteolytic processing involved in the release of fragment A from the intact fusion toxin mol.

=> s l2 and (charbohydrate or galact?)
L4 14962 l2 AND (CHARBOHYDRATE OR GALACT?)

=>
=> s l2 and (carbohydrate or galact?)
L5 32129 l2 AND (CARBOHYDRATE OR GALACT?)

=> s DIPHTHERIA AND B AND BIND? and (carbohydrate or galact?)
L6 25 DIPHTHERIA AND B AND BIND? AND (CARBOHYDRATE OR GALACT?)

=> d ti 1-25

L6 ANSWER 1 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI Efficient extracellular production of recombinant Escherichia coli heat-labile enterotoxin B subunit by using the expression/secretion system of Bacillus brevis and its mucosal immunoadjuvanticity.

L6 ANSWER 2 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI CLONING NUCLEOTIDE SEQUENCE AND HYBRIDIZATION STUDIES OF THE TYPE IIB HEAT-LABILE ENTEROTOXIN GENE OF ESCHERICHIA-COLI.

L6 ANSWER 3 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI IMMUNO TOXINS HYBRID MOLECULES OF MONO CLONAL ANTIBODIES AND A TOXIN SUBUNIT SPECIFICALLY KILL TUMOR CELLS.

L6 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI RICIN LINKED TO MONO PHOSPHO PENTA MANNOSE **BINDS** TO FIBROBLAST LYSOSOMAL HYDROLASE RECEPTORS RESULTING IN A CELL TYPE SPECIFIC TOXIN.

L6 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Gene profiling methods of diagnosing potential for metastasis or developing hepatocellular carcinoma and of identifying therapeutic targets

L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Gene expression profiles for diagnostic and prognostic grading of breast cancer and for drug screening

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Effects of iron limitation on adherence and cell surface carbohydrates of Corynebacterium diphtheriae strains

L6 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Methods for production of biochips and their use in cancer diagnosis and treatment

L6 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Modular biochip arrays and their diagnostic or analytical uses and their preparation and uses

L6 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Synthetic pre-trans-splicing molecules (PTM) encoding diptheria toxin subunit A used for double RNA trans-splicing to disrupt human papillomavirus virus 16 genes for cervix carcinoma treatment

L6 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes

L6 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Expression vector system and a method for optimization and confirmation of DNA delivery and quantification of targeting frequency

L6 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI A mammalian two-hybrid system for adenomatous polyposis coli-mutated colon cancer therapeutics

L6 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Albumin fusion proteins with therapeutic proteins for improved shelf-life

L6 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Glycoprotein antigens, antibodies specific thereto and method for producing same

L6 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Efficient extracellular production of recombinant Escherichia coli heat-labile enterotoxin B subunit by using the expression/secretion system of Bacillus brevis and its mucosal immunoadjuvanticity

L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Novel methods for therapeutic vaccination

L6 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Immunotoxins for preventing anti-Gal production in xenograft recipients

L6 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Immunoglobulin molecules having a synthetic variable region and modified specificity

L6 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Enhanced effects for hapten conjugated therapeutics

L6 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Targeted combination immunotherapy of cancer

L6 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Reaction columns for simultaneous multiple measurements and method for determination of compounds

L6 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Antibodies and autoantigen and methods for diagnosis and treatment of insulin-dependent diabetes mellitus

L6 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Covalently-linked complexes and methods for enhanced cytotoxicity and imaging

L6 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
TI Cloning, nucleotide sequence, and hybridization studies of the type IIb heat-labile enterotoxin gene of Escherichia coli

=> d bib abs 4 25

L6 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 1980:184155 BIOSIS
DN PREV198069059151; BA69:59151
TI RICIN LINKED TO MONO PHOSPHO PENTA MANNOSE **BINDS** TO FIBROBLAST LYSOSOMAL HYDROLASE RECEPTORS RESULTING IN A CELL TYPE SPECIFIC TOXIN.
AU YOULE R J [Reprint author]; MURRAY G J; NEVILLE D M JR
CS SECT BIOPHYS CHEM, LAB NEUROCHEM, NATL INST MENT HEALTH, BETHESDA, MD

20205, USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1979) Vol. 76, No. 11, pp. 5559-5562.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
FS BA
LA ENGLISH
AB The receptor specificity of the plant seed toxin ricin, which ordinarily **binds** to **galactose**-containing receptors, was altered by coupling monophosphopentamannose residues to ricin by reductive amination and by reversibly **binding** lactose to the modified ricin. The added monophosphopentamannose residues provide ricin with the recognition factor common to fibroblast lysosomal hydrolases and enable the modified ricin (Man6P-ricin) to **bind** to the fibroblast Man6P receptor and inhibit protein synthesis in the cells via this receptor. The addition of lactose to Man6P-ricin saturates the **galactose** site on Man6P-ricin and prevents the **binding** of Man6P-ricin to cells via **galactose**-containing ricin receptors. The Man6P receptor-mediated toxicity of Man6P-ricin, identified in human fibroblasts by competition by Man6P and blockade by alkaline phosphatase treatment, was not detected in HeLa cells or human amnion cells. In the presence of lactose, the fibroblasts were 8 and 13 times more sensitive than amnion and HeLa cells, respectively. Highly toxic cell-type-specific reagents can be made by the proper alteration of toxin receptor specificities. An attempt to construct a highly toxic altered toxin by adding Man6P residues to **diphtheria** toxin fragment A was unsuccessful. A possible explanation is that in Man6P-ricin the ricin **B** chain performs some entry function, even though the initial **binding** step occurs at the Man6P receptor. The present work is a further attempt to construct a cell-type-specific cytotoxic reagent with potential antineoplastic activity utilizing the concepts previously developed for artificial hybrid proteins.

L6 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
AN 1990:173143 CAPLUS
DN 112:173143
TI Cloning, nucleotide sequence, and hybridization studies of the type IIb heat-labile enterotoxin gene of Escherichia coli
AU Pickett, Carol L.; Twiddy, Edda M.; Coker, Christopher; Holmes, Randall K.
CS Dep. Microbiol., Unif. Serv. Univ. Health Sci., Bethesda, MD, 20814, USA
SO Journal of Bacteriology (1989), 171(9), 4945-52
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English
AB Type IIb heat-labile enterotoxin (LT-IIb) is produced by E. coli 41. Restriction fragments of total cell DNA from strain 41 were cloned into a cosmid vector, and one cosmid clone that encoded LT-IIb was identified. The genes for LT-IIb were subcloned into a variety of plasmids, expressed in minicells, sequenced, and compared with the structural genes for other members of the Vibrio cholerae-E. coli enterotoxin family. The A subunits of these toxins all have similar ADP-ribosyltransferase activity. The A genes of LT-IIa and LT-IIb exhibited 71% DNA sequence homol. with each other and 55 to 57% homol. with the A genes of cholera toxin (CT) and the type I enterotoxins of E. coli (LTh-I and LTp-I). The A subunits of the heat-labile enterotoxins also have limited homol. with other ADP-ribosylating toxins, including pertussis toxin, **diphtheria** toxin, and Pseudomonas aeruginosa exotoxin A. The **B** subunits of LT-IIa and LT-IIb differ from each other and frame type I enterotoxins in their **carbohydrate-binding** specificities. The **B** genes of LT-IIa and LT-IIb were 66% homologous, but neither had significant homol. with the **B** genes of CT, LTh-I, and LTp-I. The A subunit genes for the type I and type II enterotoxins represent distinct branches of an evolutionary tree, and the divergence between the A subunit genes of LT-IIa and LT-IIb is greater than that between CT and LT-I. In contrast, it has not yet been possible to demonstrate an evolutionary relationship between the **B** subunits of type I and type II heat-labile enterotoxins. Hybridization studies with DNA from independently isolated LT-II producing strains of E. coli also suggested that addnl. variants of LT-II exist.

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L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2003:835989 CAPLUS
TI Effects of iron limitation on adherence and cell surface carbohydrates of Corynebacterium diphtheriae strains
AU Moreira, Lilian de Oliveira; Andrade, Arnaldo Feitosa Braga; Andrade, Braga; Vale, Marcio Damasceno; Souza, Sonia Maria Silva; Hirata, Raphael, Jr.; Asad, Lidia Maria Oliveira Buarque; Asad, Nasser Ribeiro; Monteiro-Leal, Luiz Henrique; Previato, Jose Osvaldo; Mattos-Guaraldi, Ana Luiza
CS Faculdade de Ciencias Medicas, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil
SO Applied and Environmental Microbiology (2003), 69(10), 5907-5913

CODEN: AEMIDF; ISSN: 0099-2240
PB American Society for Microbiology
DT Journal
LA English
AB Iron limitation may cause bacterial pathogens to grow more slowly; however, it may also stimulate these microorganisms to produce greater tissue damage, given that many virulence factors are controlled by the iron supply in the environment. The present study investigated the influence of low iron availability on the expression of proteins and surface sugar residues of two toxigenic strains of Corynebacterium diphtheriae subsp. mitis and evaluated their adherence to human group B erythrocytes and HEp-2 cells. A comparison was made between bacteria grown in (i) Trypticase soy broth (TSB), (ii) TSB treated with dipyridyl to deplete free iron, and (iii) TSB enriched with FeCl3. The effects of iron concn. on adhesive properties were different for strains 241 and CDC-E8392, of the sucrose-fermenting and non-sucrose-fermenting biotypes, resp. Iron-limited conditions enhanced interaction of strain 241 with erythrocytes and HEp-2 cells. Inhibition assays suggested the involvement of nonfimbrial protein combination 67-72p on hemagglutination of **diphtheria** bacilli grown under iron-limited conditions. Conversely, iron limitation inhibited adherence to glass and expression of electron-dense material on the bacterial surface. Lectin **binding** assays demonstrated a redn. in the no. of sialic acid residues and an increase in D-mannose and D-**galactose** residues on the surfaces of both strains. Thus, iron exerts a regulatory role on adhesive properties of **diphtheria** bacilli, and low iron availability modulates the expression of C. diphtheriae surface **carbohydrate** moieties. The significant changes in the degree of lectin **binding** specific for D-mannose, D-**galactose** and sialic acid residues may have an effect on **binding** of host cells. The expression of dissimilar microbial virulence determinants may be coordinately controlled by common regulatory systems. For C. diphtheriae, the present results imply regulation of adherence and slime prodn. as part of a global response to iron-limited environmental conditions that includes derepression of genes for the synthesis of cytotoxin and siderophores and for transport of the Fe(III)-siderophore complexes.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2000:240985 CAPLUS
DN 132:292701
TI Novel methods for therapeutic vaccination
IN Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla
PA M & E Biotech A/S, Den.
SO PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020027	A2	20000413	WO 1999-DK525	19991005
	WO 2000020027	A3	20001012		
	W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2345817	AA	20000413	CA 1999-2345817	19991005
	AU 9958510	A1	20000426	AU 1999-58510	19991005
	AU 751709	B2	20020822		
	EP 1117421	A2	20010725	EP 1999-945967	19991005
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO				
	JP 2002526419	T2	20020820	JP 2000-573386	19991005
	EE 200100203	A	20021015	EE 2001-203	19991005
	NO 2001001586	A	20010531	NO 2001-1586	20010328
	ZA 2001002603	A	20020930	ZA 2001-2603	20010329
	HR 2001000319	A1	20020630	HR 2001-319	20010504
PRAI	DK 1998-1261	A	19981005		
	US 1998-105011P	P	19981020		
	WO 1999-DK525	W	19991005		

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably

self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

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